General

Guideline Title

Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over.

Bibliographic Source(s)

National Collaborating Centre for Cancer. Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb 10. 15 p. (NICE guideline; no. 36).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Recommendations

Major Recommendations

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

The wording used in the recommendations in this guideline (for example, words such as 'offer' and 'consider') denotes the certainty with which the recommendation is made (the strength of the recommendation) and is defined at the end of the "Major Recommendations" field.

Information and Support

Information Needs

For people with cancer of the upper aerodigestive tract and their carers:

- Provide consistent information and support at diagnosis.
- Review their needs throughout the care pathway including at the end of treatment.
- Tailor information and support to the person's needs (including the benefits and side effects of treatment, psychosocial and long-term functional issues).

Give people contact details for their allocated key worker, in line with the NICE service guidance on improving outcomes in head and neck cancer and recommendations of the National Peer Review Programme.

Give people details of peer support services that can help them throughout their care pathway.

Offer information about human papillomavirus (HPV) to people with HPV-related cancer of the upper aerodigestive tract.

Smoking Cessation

Inform patients and carers at the point of diagnosis about how continuing to smoke adversely affects outcomes such as:

- Treatment-related side effects
- Risk of recurrence
- Risk of second primary cancers

Offer help to people to stop smoking, in line with the NICE guideline on stop smoking services .

Investigation

Assessment of Neck Lumps

Consider adding ultrasound guidance to fine-needle aspiration cytology or core biopsy for people with a neck lump that is suspected of being cancer of the upper aerodigestive tract.

Consider having a cytopathologist or biomedical scientist assess the cytology sample adequacy when the procedure is carried out.

Identifying the Occult Primary

Consider a fluorodeoxyglucose positron emission tomography (FDG PET)-computed tomography (CT) scan as the first investigation to detect the primary site in people with metastatic nodal squamous cell carcinoma of unknown origin that is thought to arise from the upper aerodigestive tract.

Consider using narrow-band imaging endoscopy to identify a possible primary site when it has not been possible to do so using FDG PET-CT.

Offer a biopsy to confirm a possible primary site.

Offer surgical diagnostic assessment if FDG PET-CT does not identify a possible primary site. This may include:

- Guided biopsies
- Tonsillectomy
- Tongue base mucosectomy

Consider a magnetic resonance image (MRI) or CT scan before diagnostic surgery to help with radiotherapy treatment planning.

Clinical Staging – Who and How?

Offer systemic staging (see recommendations below) to all people with cancer of the upper aerodigestive tract except those with T1N0 or T2N0 disease.

Offer FDG PET-CT to people with T4 cancer of the hypopharynx or nasopharynx.

Offer FDG PET-CT to people with N3 cancer of the upper aerodigestive tract.

Offer conventional imaging (for example, chest CT) to people with cancer of the upper aerodigestive tract who require systemic staging (see recommendation above) but FDG PET-CT is not indicated for them.

Treatment of Early Stage Disease

Squamous Cell Carcinoma of the Larynx

Offer transoral laser microsurgery to people with newly diagnosed T1a squamous cell carcinoma of the glottic larynx.

Offer a choice of transoral laser microsurgery or radiotherapy to people with newly-diagnosed T1b–T2 squamous cell carcinoma of the glottic larynx.

Offer a choice of transoral surgery or radiotherapy to people with newly-diagnosed T1–T2 squamous cell carcinoma of the supraglottic larynx.

Management of the N0 Neck in T1–2 Squamous Cell Carcinoma of the Oral Cavity

Offer surgical management of the neck to all people with early oral cavity cancer (T1–T2, N0).

Offer sentinel lymph node biopsy instead of elective neck dissection to people with early oral cavity cancer (T1–T2, N0), unless they need cervical access at the same time (for example, free-flap reconstruction).

Squamous Cell Carcinoma of the Oropharynx (T1–2, N0)

Offer people the choice of transoral surgical resection or primary radiotherapy for T1–2 N0 tumours of the oropharynx.

Consider postoperative radiotherapy, with or without concomitant chemotherapy, for T1–2 N0 tumours of the oropharynx if pathologically adverse risk factors have been identified.

Treatment of Advanced Disease

Squamous Cell Carcinoma of the Larynx

Offer people with T3 squamous cell carcinoma of the larynx a choice of:

- Radiotherapy with concomitant chemotherapy, or
- Surgery with adjuvant radiotherapy, with or without concomitant chemotherapy

Discuss the following with people with T3 squamous cell carcinoma of the larynx and their carers, to inform their choice of treatment:

- The potential advantages of laryngeal preservation
- The risk of needing salvage laryngectomy (and its associated complications)
- The benefits of primary surgery in people with existing compromised swallowing and airway function
- Likely voice and swallowing function after treatment (including the need for a long-term feeding tube)

For people with T4a squamous cell carcinoma of the larynx consider surgery with adjuvant radiotherapy, with or without concomitant chemotherapy.

Squamous Cell Carcinoma of the Hypopharynx

Offer larynx-preserving treatment to people with locally-advanced squamous cell carcinoma of the hypopharynx if radiation and neo-adjuvant and/or concomitant chemotherapy would be suitable for them and they do not have:

- Tumour-related dysphagia needing a feeding tube
- A compromised airway
- Recurrent aspiration pneumonias

Offer radiotherapy with neo-adjuvant and/or concomitant chemotherapy if larynx-preserving treatment is suitable for the person.

Offer primary surgery followed by adjuvant radiotherapy to people if chemotherapy is not a suitable treatment for them.

Offer adjuvant radiotherapy to people having surgery as their primary treatment. Add concomitant chemotherapy if appropriate.

Palliation of Breathing Difficulties

Identify people at risk of airways obstruction for whom intervention is appropriate. Think about:

- Their performance status
- Treatment side effects and length of hospital stay
- Involving the palliative care team and other specialists when appropriate

Consider endoluminal debulking in preference to tracheostomy.

Establish a management plan if surgical intervention is not appropriate, in conjunction with the person, carers and clinical staff.

Assess and treat other causes of breathlessness in people with incurable upper aerodigestive tract cancer.

HPV-related Disease

HPV Testing

Test all squamous cell carcinomas of the oropharynx using p16 immunohistochemistry. Regard the p16 test result as positive only if there is strong nuclear and cytoplasmic staining in more than 70% of tumour cells.

Consider high-risk HPV deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) in-situ hybridisation in all p16-positive cancers of the oropharynx to confirm HPV status.

De-Intensification of Treatment

Do not offer de-intensification of curative treatment to people with HPV-positive cancer of the oropharynx, unless it is part of a clinical trial.

Less Common Upper Aerodigestive Tract Cancers

Carcinoma of the Nasopharynx

Offer intensity-modulated radiation therapy with concomitant chemotherapy to people with locally-advanced (stage II and above) nasopharyngeal cancer.

Consider adjuvant or neo-adjuvant chemotherapy for people with locally-advanced (stage II and above) nasopharyngeal cancer.

Carcinoma of the Paranasal Sinuses

Offer surgery as the first treatment for carcinoma of the paranasal sinuses if complete resection is possible.

Consider radiotherapy with or without concomitant chemotherapy before planned surgical resection of the paranasal sinuses if complete resection is not initially possible.

Unknown Primary of Presumed Upper Aerodigestive Tract Origin

Offer people with squamous cell carcinoma in the cervical lymph nodes with an unknown primary the choice of:

- Neck dissection and adjuvant radiation with or without chemotherapy, or
- Primary radiation with or without chemotherapy, with surgery for persistent disease

Consider no further treatment as an option in people with pN1 disease without extracapsular spread after neck dissection.

Consider including potential primary tumour sites when selecting the volume to be treated with radiotherapy.

Mucosal Melanoma

Consider surgery and adjuvant radiotherapy for people with newly-diagnosed upper aerodigestive tract mucosal melanoma without systemic metastases.

Optimising Rehabilitation and Function

Enteral Nutrition Support

Assess people's need for enteral nutrition at diagnosis, including prophylactic tube placement. The multidisciplinary team should take into account:

- Performance status and social factors
- Nutritional status (weight loss, high or low body mass index [BMI], ability to meet estimated nutritional needs)
- Tumour stage
- Tumour site
- Pre-existing dysphagia
- Impact of planned treatment (such as radiation treatment volume and dose-fractionation, concomitant chemotherapy, and extent and site of surgery)

Follow the recommendations in NICE's guideline on nutrition support for adults for people aged 18 years and over.

Speech and Language Therapy Interventions

Consider swallowing-exercise programmes for people having radiotherapy.

Consider mouth-opening exercises for people having radiotherapy who are at risk of reduced mouth opening.

Consider voice therapy for people whose voice has changed because of their treatment.

Shoulder Rehabilitation

Consider progressive resistance training for people with impaired shoulder function, as soon as possible after neck dissection.

Follow-up of People with Cancer of the Upper Aerodigestive Tract and Management of Osteoradionecrosis

Follow-up

Ensure people with cancer of the upper aerodigestive tract and their carers have tailored information about the symptoms of recurrence and late effects of treatment at the end of curative therapy.

Consider structured, risk-adapted follow-up using locally-agreed protocols for people who have had curative treatment for cancer of the upper aerodigestive tract. Use the follow-up protocols to:

- Help improve quality of life, including discussing psychosocial issues
- Detect disease recurrence or second primary cancer, possibly including narrow-band imaging to improve detection

Management of Osteoradionecrosis

Consider surgery to remove necrotic bone and to establish soft tissue coverage in people with osteoradionecrosis.

Only consider hyperbaric oxygen therapy or medical management for treating osteoradionecrosis as part of a clinical trial.

Stages of Upper Aerodigestive Tract Cancer

The stages of upper aerodigestive tract cancer referred to in this guideline are listed below.

- T0: this means there is no primary tumour, but there may be abnormal cells that are precancerous.
- T1 to T4: this refers to the increasing size and/or extent of the primary tumour, with 1 being smallest and 4 largest.
- N0: no lymph nodes contain cancer cells.
- N1 and upwards: increasing involvement of lymph nodes by cancer cells.

Definitions

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee (GC) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GC is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GC usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally the GC uses 'must' (or 'must not') if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GC uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. The GC uses similar forms of words (for example, 'Do not offer…') when confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GC uses 'consider' when the GC is confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Clinical Algorithm(s)

A pictorial representation of the diagnostic recommendations is provided in the full version of the guideline (see the "Availability of Companion Documents" field).

In addition, a National Institute for Health and Care Excellence (NICE) pathway titled "Upper aerodigestive tract cancer overview" is available from the NICE Web site .

Scope

Disease/Condition(s)

Cancer of the upper aerodigestive tract (oral cavity, oropharynx, nasopharynx, hypopharynx, larynx, and paranasal sinuses)

Guideline Category

Diagnosis

Evaluation

Management

Treatment

Clinical Specialty

Family Practice

Internal Medicine

Nutrition

Oncology

Otolaryngology

Radiation Oncology

Speech-Language Pathology

Intended Users

Advanced Practice Nurses

Dietitians

Health Care Providers

Nurses

Physician Assistants

Physicians

Speech-Language Pathologists

Guideline Objective(s)

To provide a clinical guideline on the assessment and management of upper airways tract cancers

Target Population

- Adults and young people (16 years and older) referred from primary care with suspected cancer of the upper airways tract
- Adults and young people (16 years and older) with newly diagnosed or recurrent cancer of the upper airways tract

Note: The guideline will not cover:

- Adults and young people with cancers of the thyroid, orbit, middle ear, cutaneous lip, skull base or salivary gland
- Adults and young people with sarcoma or lymphoma
- Children and young people under 16 years

Interventions and Practices Considered

1. Providing information and support
2. Offering help to stop smoking
3. Assessment of neck lumps using ultrasound guidance and fine-needle aspiration cytology of core biopsy
4. Identifying the occult primary
    - Fluorodeoxyglucose positron emission tomography (FDG PET)-computed tomography (CT)
    - Narrow-band imaging endoscopy
    - Biopsy
    - Guided biopsies
    - Tonsillectomy
    - Tongue base mucosectomy
    - Magnetic resonance imaging (MRI) or CT scan before diagnostic surgery
5. Systematic clinical staging (FDG PET-CT or conventional imaging [e.g., CT])
6. Management of early-stage squamous cell carcinoma of the larynx
    - Transoral laser microsurgery
    - Radiotherapy
7. Management of the N0 neck in early-stage T1–2 squamous cell carcinoma of the oral cavity
    - Surgical management
    - Sentinel lymph node biopsy
8. Management of squamous cell carcinoma of the oropharynx (T1–2, N0)
    - Transoral surgical resection
    - Primary radiotherapy
    - Postoperative radiotherapy, with or without concomitant chemotherapy
9. Management of advanced squamous cell carcinoma of the larynx
    - Radiotherapy with concomitant chemotherapy
    - Surgery with adjuvant radiotherapy, with or without concomitant chemotherapy
10. Management of advance squamous cell carcinoma of the hypopharynx
    - Larynx-preserving treatment
    - Radiotherapy with neo-adjuvant and/or concomitant chemotherapy
    - Primary surgery followed by adjuvant radiotherapy
    - Adjuvant radiotherapy for people having surgery as their primary treatment with concomitant chemotherapy if appropriate
11. Palliation of breathing difficulties
    - Identifying people at risk of airways obstruction for whom intervention is appropriate
    - Endoluminal debulking (in preference to tracheostomy)
    - Establishing a management plan
    - Assessing and treating other causes of breathlessness
12. Management of human papillomavirus (HPV)-related disease
    - HPV testing

    - High-risk HPV deoxyribonucleic acid (DNA) or ribonucleic acid (RNA) in-situ hybridisation
    - De-intensification of treatment (recommended only as part of a clinical trial)
13. Management of less common upper aerodigestive tract cancers (carcinoma of the nasopharynx, carcinoma of the paranasal sinuses, unknown primary tumour of presumed aerodigestive tract origin, mucosal melanoma)
14. Optimising rehabilitation and function
    - Enteral nutrition support
    - Speech and language therapy interventions
    - Shoulder rehabilitation
15. Follow-up
16. Management of osteoradionecrosis

Major Outcomes Considered

- Overall survival
- Disease-free survival
- Disease-related morbidity
- Treatment-related morbidity and mortality
- Diagnostic accuracy
- Number and length of admissions to hospital after diagnosis
- Health-related quality of life
- Cost-effectiveness

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C) on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

Developing Clinical Evidence-Based Questions

Background

Clinical guidelines should be aimed at changing clinical practice and should avoid ending up as 'evidence-based textbooks' or making recommendations on topics where there is already agreed clinical practice. Therefore the list of key clinical issues listed in the scope were developed for areas that were known to be controversial or uncertain, where there was identifiable practice variation, or where NICE guidelines were likely to have most impact.

Method

From each of the key clinical issues identified in the scope, the Guideline Committee (GC) formulated a clinical question. For clinical questions about interventions, the PICO framework was used. This structured approach divides each question into four components: P – the population (the population under study); I – the interventions (what is being done); C – the comparison (other main treatment options); O – the outcomes (the measures of how effective the interventions have been).

Review of Clinical Literature

Scoping Search

An initial scoping search for published guidelines, systematic reviews, economic evaluations and ongoing research was carried out on the following databases or Web sites: National Health Service (NHS) Evidence, NICE, Cochrane Databases of Systematic Reviews (CDSR), Health Technology Assessment Database (HTA), TRIP (Turning Research into Practice), Scottish Intercollegiate Guidelines Network (SIGN), NHS Economic Evaluations Database (NHSEED), Health Economic Evaluations Database (HEED), Medline and EMBASE.

At the beginning of the development phase, initial scoping searches were carried out to identify any relevant guidelines (local, national or international) produced by other groups or institutions.

Developing the Review Protocol

For each clinical question, the information specialist and researcher (with input from other technical team and GC members) prepared a review protocol. This protocol explains how the review was to be carried out (see Table 1 in the full version of the guideline) in order to develop a plan of how to review the evidence, limit the introduction of bias and for the purposes of reproducibility. All review protocols can be found in the evidence review (see Appendix H).

Searching for the Evidence

In order to answer each question the NCC-C information specialist developed a search strategy to identify relevant published evidence for both clinical and cost effectiveness. Key words and terms for the search were agreed in collaboration with the GC.

Search filters, such as those to identify systematic reviews (SRs) and randomised controlled trials (RCTs) were applied to the search strategies when necessary. No language restrictions were applied to the search; however, foreign language papers were not requested or reviewed (unless of particular importance to that question).

The following databases were included in the literature search:

- The Cochrane Library
- Medline and Premedline 1946 onwards
- Excerpta Medica (EMBASE) 1974 onwards
- Web of Science (specifically Science Citation Index Expanded [SCI-Expanded] 1900 onwards, Social Sciences Citation Index [SSCI] 1900 onwards and Conference Proceedings Citation Index - Science [CPCI-S] 1990-present

Subject specific databases used for certain topics:

- Cumulative Index to Nursing and Allied Health Literature (CINAHL) 1937 onwards
- PsycINFO 1806 onwards

From this list the information specialist sifted and removed any irrelevant material based on the title or abstract before passing to the researcher. All the remaining articles were then stored in a Reference Manager electronic library.

Searches were updated and re-run 6 to 8 weeks before the guideline was submitted to NICE for stakeholder consultation, thereby ensuring that the latest relevant published evidence was included in the database. Any evidence published after this date was not included. For the purposes of updating this guideline, June 2015 should be considered the starting point for searching for new evidence.

Further details of the search strategies, including the methodological filters used, are provided in the evidence review.

Critical Appraisal

Following the literature search one researcher independently scanned the titles and abstracts of every article for each question, and full publications were obtained for any studies considered relevant or where there was insufficient information from the title and abstract to make a decision. When papers were obtained the researcher applied inclusion/exclusion criteria to select appropriate studies, which were then critically appraised. If results from a study were published as more than one paper, the most recent or complete publication was used.

Incorporating Health Economics Evidence

The aim of providing economic input into the development of the guideline was to inform the GC of potential economic issues relating to upper aerodigestive tract cancer. Health economics is about improving the health of the population through the efficient use of resources. In addition to assessing clinical effectiveness, it is important to investigate whether health services are being used in a cost effective manner in order to maximise health gain from available resources.

Prioritising Topics for Economic Analysis

After the clinical questions had been defined, and with the help of the health economist, the GC discussed and agreed which of the clinical questions were potential priorities for economic analysis. These economic priorities were chosen on the basis of the following criteria, in broad accordance with the NICE guidelines manual (NICE 2012) (see the "Availability of Companion Documents" field):

- The overall importance of the recommendation, which may be a function of the number of patients affected and the potential impact on costs and health outcomes per patient
- The current extent of uncertainty over cost effectiveness, and the likelihood that economic analysis will reduce this uncertainty
- The feasibility of building an economic model

A review of the economic literature was conducted at scoping. Where published economic evaluation studies were identified that addressed the economic issues for a clinical question, these are presented alongside the clinical evidence.

For systematic searches of published economic evidence, the following databases were included:

- Medline
- EMBASE
- NHS EED
- HTA
- HEED

Number of Source Documents

See the "Clinical Evidence" sections for each clinical question in the full version of the guideline and Appendix H in the full guideline appendices (see the "Availability of Companion Documents" field) for details regarding the number and type of included studies.

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Overall Quality Evidence in Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Quality Element	Description
High	Further research is very unlikely to change confidence in the estimate of effect.
Moderate	Further research is likely to have an important impact on confidence in the estimate of effect and may change the estimate.
Low	Further research is very likely to have an important impact on confidence in the estimate of effect and is likely to change the estimate.
Very low	Any estimate of effect is very uncertain.

Methods Used to Analyze the Evidence

Meta-Analysis

Systematic Review with Evidence Tables

Description of the Methods Used to Analyze the Evidence

Note from the National Guideline Clearinghouse (NGC): This guideline was developed by the National Collaborating Centre for Cancer (NCC-C)

on behalf of the National Institute for Health and Care Excellence (NICE). See the "Availability of Companion Documents" field for the full version of this guidance and related appendices.

Review of the Clinical Literature

Critical Appraisal and Evidence Grading

For each question, data were extracted on the outcomes identified as critical or important by the Guideline Committee (GC) and recorded in evidence tables and an accompanying evidence summary prepared for the GC. All evidence was considered carefully by the GC for accuracy and completeness.

Grading of Recommendations Assessment, Development and Evaluation (GRADE)

For interventional questions, studies which matched the inclusion criteria were evaluated and presented using GRADE (NICE 2012; http://gradeworkinggroup.org/). Where possible this included meta-analysis and synthesis of data into a GRADE 'evidence profile'. The evidence profile shows, for each outcome, an overall assessment of both the quality of the evidence as a whole (very low, low, moderate or high) as well as an estimate of the size of effect. A narrative summary (evidence statement) was also prepared.

Each outcome was examined for the quality elements defined in Table 2 in the full version of the guideline and subsequently graded using the quality levels listed in the "Rating Scheme for the Strength of the Evidence" field. The reasons for downgrading or upgrading specific outcomes were explained in footnotes.

All procedures were fully compliant with NICE methodology as detailed in the 'NICE guidelines manual' (NICE 2012) (see the "Rating Scheme for the Strength of the Evidence" field). In general, evidence was based on published data only. Study authors were contacted only to resolve any ambiguities, such as unclear presentation of data, or where clarification was needed in order to include or exclude a paper in the evidence review.

For non-interventional questions, for example questions regarding diagnostic test accuracy, a narrative summary of the quality of the evidence was provided. The quality of individual diagnostic accuracy studies was assessed using the QUADAS-2 tool.

Incorporating Health Economics Literature

Methods for Reviewing and Appraising Economic Evidence

The aim of reviewing and appraising the existing economic literature is to identify relevant economic evaluations that compare both costs and health consequences of alternative interventions and that are applicable to National Health Service (NHS) practice. Thus studies that only report costs, non-comparative studies of 'cost of illness' studies are generally excluded from the reviews.

Economic studies identified through a systematic search of the literature are appraised using a methodology checklist designed for economic evaluations. This checklist is not intended to judge the quality of a study per se, but to determine whether an existing economic evaluation is useful to inform the decision-making of the GC for a specific topic within the guideline. There are two parts of the appraisal process; the first step is to assess applicability (i.e., the relevance of the study to the specific guideline topic and the NICE reference case) (see Table 4 in the full version of the guideline for applicability criteria).

In the second step, only those studies deemed directly or partially applicable are further assessed for limitations (i.e., the methodological quality, see Table 5 in the full version of the guideline).

Where relevant, a summary of the main findings from the systematic search, review and appraisal of economic evidence is presented in an economic evidence profile alongside the clinical evidence.

If high-quality published economic evidence relevant to current NHS practice was identified through the search, the existing literature was reviewed and appraised as described above. However, it is often the case that published economic studies may not be directly relevant to the specific clinical question as defined in the guideline or may not be comprehensive or conclusive enough to inform UK practice. In such cases, for priority topics, consideration was given to undertaking a new economic analysis as part of this guideline.

Economic Modelling

Once the need for a new economic analysis for high priority topics had been agreed by the GC, the health economist investigated the feasibility of developing an economic model. In the development of the analysis, the following general principles were adhered to:

- The GC subgroup was consulted during the construction and interpretation of the analysis
- The analysis was based on the best available clinical evidence from the systematic review

- Assumptions were reported fully and transparently
- Uncertainty was explored through sensitivity analysis
- Costs were calculated from a health services perspective
- Outcomes were reported in terms of quality-adjusted life years

Methods Used to Formulate the Recommendations

Expert Consensus

Informal Consensus

Description of Methods Used to Formulate the Recommendations

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The Guideline Development Process – Who Develops the Guideline?

Overview

The development of this guideline was based upon methods outlined in the 'NICE guidelines manual' (NICE 2012 and NICE 2014 [see the "Availability of Companion Documents" field]). A team of health professionals, lay representatives and technical experts known as the Guideline Committee (GC) (see Appendix G), with support from the NCC-C staff, undertook the development of this clinical guideline. The basic steps in the process of developing a guideline are listed below:

- Using the remit, define the scope which sets the inclusion/exclusion criteria of the guideline
- Forming the GC
- Developing clinical questions
- Identifying the health economic priorities
- Developing the review protocols
- Systematically searching for the evidence
- Critically appraising the evidence
- Incorporating health economic evidence
- Distilling and synthesising the evidence and writing recommendations
- Agreeing the recommendations
- Structuring and writing the guideline
- Consultation and validation

The Scope

The scope was drafted by the GC Chair and Lead Clinician and staff at the NCC-C in accordance with processes established by NICE (NICE 2012). The purpose of the scope was to:

- Set the boundaries of the development work and provide a clear framework to enable work to stay within the priorities agreed by NICE and the NCC-C
- Inform professionals and the public about the expected content of the guideline
- Provide an overview of the population and healthcare settings the guideline would include and exclude
- Specify the key clinical issues that will be covered by the guideline
- Inform the development of the clinical questions and search strategies

Before the guideline development process started, the draft scope was presented and discussed at a stakeholder workshop. The list of key clinical issues were discussed and revised before the formal consultation process. Further details of the discussion at the stakeholder workshop can be found on the NICE Web site .

The scope was subject to a four-week stakeholder consultation in accordance with NICE processes. The full scope is shown in Appendix F.

During the consultation period, the scope was posted on the NICE Web site. Comments were invited from registered stakeholder organisations and NICE staff. The NCC-C and NICE reviewed the scope in light of comments received, and the revised scope was reviewed and signed off by NICE and posted on the NICE Web site.

The Guideline Committee (GC)

The upper aerodigestive tract cancer GC was recruited in line with the 'NICE guidelines manual' (NICE 2012). The first step was to appoint a Chair and a Lead Clinician. Advertisements were placed for both posts and shortlisted candidates were interviewed in person prior to being offered the role. The NCC-C Director, GC Chair and Lead Clinician identified a list of specialties that needed to be represented on the GC. Details of the adverts were sent to the main stakeholder organisations, cancer networks and patient organisations/charities (see Appendix G). Individual GC members were selected for telephone interview by the NCC-C Director, GC Chair and Lead Clinician, based on their application forms. The guideline development process was supported by staff from the NCC-C, who undertook the clinical and health economics literature searches, reviewed and presented the evidence to the GC, and managed the process and contributed to drafting the guideline.

Guideline Committee Meetings

Thirteen GC meetings were held between 16–17 Dec 2013 and 2–3 Nov 2015. During each GC meeting (held over either one or two days) clinical questions and clinical and economic evidence were reviewed, assessed and recommendations formulated. At each meeting patient/carer and service-user concerns were routinely discussed as part of a standing agenda item.

NCC-C project managers divided the GC workload by allocating specific clinical questions, relevant to their area of clinical practice, to small sub-groups of the GC in order to simplify and speed up the guideline development process. These groups considered the evidence, as reviewed by the researcher, and synthesised it into draft recommendations before presenting it to the GC. These recommendations were then discussed and agreed by the GC as a whole. Each clinical question was led by a GC member with expert knowledge of the clinical area (usually one of the healthcare professionals). The GC subgroups often helped refine the clinical questions and the clinical definitions of treatments. They also assisted the NCC-C team in drafting the section of the guideline relevant to their specific topic.

Patient/Carer Representatives

Individuals with direct experience of upper aerodigestive tract cancer services gave an important user focus to the GC and the guideline development process. The GC included two patient/carer members. They contributed as full GC members to writing the clinical questions, helping to ensure that the evidence addressed their views and preferences, highlighting sensitive issues and terminology relevant to the guideline and bringing service-user research to the attention of the GC.

Expert Advisers

During the development of the guideline the GC identified shoulder rehabilitation following neck dissection as a topic that required additional expert input. One expert was identified by the NCC-C and GC (see Appendix G) and invited to advise the GC on drafting their recommendations for that clinical question.

Agreeing the Recommendations

For each clinical question the GC were presented with a summary of the clinical evidence, and, where appropriate, economic evidence, derived from the studies reviewed and appraised. The GC derived their guideline recommendations from this information. The link between the evidence and the view of the GC in making each recommendation is made explicitly in the accompanying Linking Evidence to Recommendations (LETR) statement (see below).

Wording of the Recommendations

The wording used in the recommendations in this guideline denotes the certainty with which the recommendations were made. Some recommendations were made with more certainty than others. Recommendations are based on the trade-off between the benefits and harms of an intervention, whilst taking into account the quality of the underpinning evidence.

For all recommendations, it is expected that a discussion will take place with the patients about the risks and benefits of the interventions, and their values and preferences. This discussion should help the patient reach a fully informed decision. Terms used within this guideline are:

- 'Offer' – for the vast majority of patients, an intervention will do more good than harm
- 'Do not offer' – the intervention will not be of benefit for most patients
- 'Consider' – the benefit is less certain, and an intervention will do more good than harm for most patients. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for an 'offer'

recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

LETR Statements

As clinical guidelines were previously formatted, there was limited scope for expressing how and why a GC made a particular recommendation from the evidence of clinical and cost effectiveness. To make this process more transparent to the reader, NICE have introduced an explicit, easily understood and consistent way of expressing the reasons for making each recommendation. This is known as the 'LETR statement' and will usually cover the following key points:

- The relative value placed on the outcomes considered
- The strength of evidence about benefits and harms for the intervention being considered
- The costs and cost effectiveness of an intervention
- The quality of the evidence
- The degree of consensus within the GC
- Other considerations – for example equalities issues

Where evidence was weak or lacking the GC agreed the final recommendations through informal consensus. Shortly before the consultation period five key research recommendations were selected by the GC for implementation and the patient algorithms were agreed.

Rating Scheme for the Strength of the Recommendations

Strength of Recommendations

Some recommendations can be made with more certainty than others. The Guideline Committee (GC) makes a recommendation based on the trade-off between the benefits and harms of an intervention, taking into account the quality of the underpinning evidence. For some interventions, the GC is confident that, given the information it has looked at, most patients would choose the intervention. The wording used in the recommendations in this guideline denotes the certainty with which the recommendation is made (the strength of the recommendation).

Interventions That Must (or Must Not) Be Used

The GC usually uses 'must' or 'must not' only if there is a legal duty to apply the recommendation. Occasionally 'must' (or 'must not') is used if the consequences of not following the recommendation could be extremely serious or potentially life threatening.

Interventions That Should (or Should Not) Be Used – a 'Strong' Recommendation

The GC uses 'offer' (and similar words such as 'refer' or 'advise') when confident that, for the vast majority of patients, an intervention will do more good than harm, and be cost effective. Similar forms of words (for example, 'Do not offer…') are used when the GC is confident that an intervention will not be of benefit for most patients.

Interventions That Could Be Used

The GC uses 'consider' when confident that an intervention will do more good than harm for most patients, and be cost effective, but other options may be similarly cost effective. The choice of intervention, and whether or not to have the intervention at all, is more likely to depend on the patient's values and preferences than for a strong recommendation, and so the healthcare professional should spend more time considering and discussing the options with the patient.

Cost Analysis

See the *Cost Effectiveness Evidence* for clinical questions in the full version of the guideline. See also Appendices A-C for cost-effectiveness analyses (see the "Availability of Companion Documents" field):

- Appendix A: The cost-effectiveness of systemic imaging for distant metastases in patients with cancer of the upper aerodigestive tract
- Appendix B: The cost-effectiveness of initial treatments for newly diagnosed T1 or T2 carcinoma of the larynx
- Appendix C: The Cost-effectiveness of management strategies for the clinically and radiologically N0 neck

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

Consultation and Validation of the Guideline

The draft of the guideline was prepared by National Collaborating Centre for Cancer (NCC-C) staff in partnership with the Guideline Committee (GC) Chair and Lead Clinician. This was then discussed and agreed with the GC and subsequently forwarded to the National Institute for Health and Care Excellence (NICE) for consultation with stakeholders.

Registered stakeholders (see Appendix G of the full version of the guideline [see the "Availability of Companion Documents" field]) had one opportunity to comment on the draft guideline which was posted on the NICE Web site between 3 September 2015 and 15 October 2015 in line with NICE methodology.

The Pre-Publication Process

An embargoed pre-publication version of the guideline was released to registered stakeholders who have signed a confidentiality form to allow them to see how their comments have contributed to the development of the guideline and to give them time to prepare for publication. The final document was then submitted to NICE for publication on their Web site. The other versions of the guideline were also discussed and approved by the GC and published at the same time.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type and quality of evidence supporting each review question are described in evidence profiles in the full version of the guideline and Appendix H (see the "Availability of Companion Documents" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate assessment and management of cancer of the upper aerodigestive tract leading to accurate diagnosis and improved patient experience and outcomes

See also the "Trade-off between clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for benefits of specific interventions.

Potential Harms

- The recommendations made for information and support may potentially lead to information overload for some patients, which may lead to increased anxiety if the information is not tailored to the individual.
- The Guideline Committee (GC) considered the potential harms of diagnostic imaging recommendations to be additional exposure to low-dose radiation in some patients, as a result of cross-sectional imaging.
- There is debate about which imaging tests usually used for systemic staging are most accurate. There are potential harms associated with these imaging tests including radiation exposure and the discovery of incidental problems which may complicate care.
- A proportion of negative sentinel lymph node biopsies (SLNBs) would be false negative (approximately 5%). These patients may require therapeutic neck dissection and may have a poorer outcome than if they had received an initial elective neck dissection. The GC believed that the benefit of less treatment significantly outweighs this small risk.
- Chemotherapy and radiotherapy-associated morbidities were considered to be potential harms of the recommendations that have been

made.

- Anticipated harms of recommendations for interventions for people at risk for airway obstruction are:
  - The need for some patients to undergo multiple debulking procedures (as opposed to a single tracheostomy)
  - In those patients with potential airways obstruction there is the potential increased patient anxiety from discussing planned treatment, which may not subsequently be needed.
- Additional chemotherapy is likely to be associated with additional toxicity.
- Increased treatment-related morbidity from radiotherapy was identified as a potential harm of the treatment recommendations.
- Potential harms associated with enteral feeding include procedure-related morbidity/mortality, skin excoriation and the psychosocial impact. Screening and assessment of patients by a dietitian from the multidisciplinary team (for suitability of the type of feeding tube and method of insertion) would help minimise these harms.
- No harms of progressive resistance training (PRT) were identified, providing exercises are followed correctly (exercises performed incorrectly could result in harm).
- The main perceived harm of recommendations for structured follow-up was a greater burden for patients due to more frequent appointments, and therefore more travel, more anxiety associated with appointments and awaiting test results, and from any false positive test results.

See also the "Trade-off between clinical benefits and harms" sections in the full version of the guideline (see the "Availability of Companion Documents" field) for additional harms of specific interventions.

Qualifying Statements

Qualifying Statements

- Healthcare professionals are expected to take National Institute for Health and Care Excellence (NICE) clinical guidelines fully into account when exercising their clinical judgement. However, the guidance does not override the responsibility of healthcare professionals to make decisions appropriate to the circumstances of each patient, in consultation with the patient and/or their guardian or carer.
- The Guideline Committee (GC) assumes that healthcare professionals will use clinical judgement, knowledge and expertise when deciding whether it is appropriate to apply these guidelines. The recommendations cited here are a guide and may not be appropriate for use in all situations. The decision to adopt any of the recommendations cited here must be made by the practitioner in light of individual patient circumstances, the wishes of the patient and clinical expertise. The National Collaborating Centre for Cancer (NCC-C) disclaims any responsibility for damages arising out of the use or non-use of these guidelines and the literature used in support of these guidelines.
- It has been impossible to cover every aspect of the patient pathway but instead the GC has concentrated on those areas where it was felt uncertainty or variation in practice currently exists. As such the guideline is not intended as an exhaustive textbook on the management of cancer of the upper aerodigestive tract. The guideline sets out recommendations that will be helpful and informative in decision-making and management of a variety of situations but cannot be a substitute for clinical judgement in a specific case.

Implementation of the Guideline

Description of Implementation Strategy

Guideline Implementation

The National Institute for Health and Care Excellence (NICE) invited stakeholders to give their responses to the following questions during consultation of the guideline:

- Which areas will have the biggest impact on practice and be challenging to implement? Please say for whom and why.
- What would help users overcome any challenges? (For example, existing practical resources or national initiatives, or examples of good practice.)

NICE will use the feedback received as well as consultation with members of the committee, engagement with relevant key partners and relevant desk research, to write a chapter which aims to help users of the guideline to get started with implementation. It will highlight up to 3 areas for attention, describing the benefits, barriers and enablers as well as signposting to any relevant resources or examples of practice that may help.

Implementation Tools

Clinical Algorithm

Foreign Language Translations

Mobile Device Resources

Patient Resources

Resources

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

End of Life Care

Getting Better

Living with Illness

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

National Collaborating Centre for Cancer. Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb 10. 15 p. (NICE guideline; no. 36).

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2016 Feb 10

Guideline Developer(s)

National Collaborating Centre for Cancer - National Government Agency [Non-U.S.]

Source(s) of Funding

The National Collaborating Centre for Cancer (NCC-C) was commissioned by the National Institute for Health and Care Excellence (NICE) to develop this guideline.

Guideline Committee

Guideline Committee (GC)

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

At the start of the guideline development process all Guideline Committee members' interests were recorded on a standard declaration form that covered consultancies, fee-paid work, share holdings, fellowships and support from the healthcare industry. At all subsequent Guideline Committee meetings, members declared new, arising conflicts of interest which were always recorded. See Appendix G in the full guideline appendices for declarations of interest of all Guideline Committee members and expert advisors to the Guideline Committee (see the "Availability of Companion Documents" field).

Guideline Status

This is the current release of the guideline.

This guideline meets NGC's 2013 (revised) inclusion criteria.

Guideline Availability

Available from the National Institute for Health and Care Excellence (NICE) Web site. Also available in ePub and eBook formats from the NICE Web site.

Availability of Companion Documents

The following are available:

- Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. Full guideline. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. 330 p. (NICE guideline; no. 36). Available from the National Institute for Health and Care Excellence (NICE) Web site .
- Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. Appendices A-G. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. 129 p. (NICE guideline; no. 36). Available from the NICE Web site .
- Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. Appendix H: evidence review. London (UK): National Institute for Health and Care Excellence (NICE); 2016 Feb. 974 p. (NICE guideline; no. 36). Available from the NICE Web site .
- Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. Baseline assessment tool. London (UK): National Institute for Health and Care Excellence; 2016 Feb. (NICE guideline; no. 36). Available from the NICE Web site .
- Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. Resource impact report. London (UK): National Institute for Health and Care Excellence; 2016 Feb. 5 p. (NICE guideline; no. 36). Available from the NICE Web site .
- Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. Learning podcast. Available from the NICE Web site .
- The guidelines manual 2012. London (UK): National Institute for Health and Care Excellence (NICE); 2012 Nov. Available from the NICE Web site .
- Developing NICE guidelines: the manual. London (UK): National Institute for Health and Care Excellence (NICE); 2014 Oct. Available from the NICE Web site .

Patient Resources

The following is available:

- Cancer of the upper aerodigestive tract: assessment and management in people aged 16 and over. Information for the public. London (UK): National Institute for Health and Care Excellence; 2016 Feb. 11 p. (NICE guideline; no. 36). Available from the National Institute for Health and Care Excellence (NICE) Web site . Also available in ePub and eBook formats from the NICE Web site . Also available in Welsh from the NICE Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better understand their health and their diagnosed disorders. By providing access to this patient information, it is not the intention of NGC to provide specific medical advice for particular patients. Rather we urge patients and their representatives to review this material and then to consult with a licensed health professional for evaluation of treatment options suitable for them as well as for diagnosis and answers to their personal medical questions. This patient information has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC Status

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